

LYMPHOEDEMA

By GERARD W. TAYLOR, M.S., F.R.C.S.

Assistant Director, Surgical Professorial Unit and Surgeon, St. Bartholomew's Hospital, London

Lymphoedema may be defined as an abnormal increase in interstitial fluid associated with lymphatic insufficiency. The mechanism of lymphoedema is more complex than a simple failure of tissue fluid removal by the faulty lymphatics. One of the main tasks of the lymphatic system is to scavenge from the tissue spaces substances of large molecular size. Lymphatic failure interferes with this function and consequently the small quantity of plasma protein that normally leaks through the capillary wall accumulates in the tissue spaces. This concentration of extra-vascular protein produces an abnormal extra-vascular osmotic force which results in interstitial water retention and clinical oedema. The protein-laden oedema fluid may also be responsible for the secondary tissue changes of fibrosis and hyperkeratosis that occur in lymphoedema and for the high incidence of cellulitis in this condition. Lymphoedema involving a major part of a limb is usually due to a fault in the major lymphatic trunks. The microscopic dermal lymphatic plexus is also subject to pathological change (Butcher and Hoover, 1955), usually secondary to chronic ulcerative or inflammatory conditions, but the clinical effect is then a purely local affair and gross subcutaneous oedema does not occur. The aetiology and pathology of certain varieties of lymphoedema remained obscure for many years because of the clinical inaccessibility of the lymphatic system. The introduction of lymphangiography (Kinmonth and Taylor, 1955) has resolved some of these problems and the following classification of lymphoedema is proposed in the light of recent knowledge.

(a) *Primary Lymphoedema*. ('Idiopathic' lymphoedema, elephantiasis nostras.)

(b) *Secondary Lymphoedema*—due to interference with lymphatic function by the following acquired lesions:—

- (1) Neoplastic invasion.
- (2) Surgical excision or radiotherapy.
- (3) Inflammation or filariasis.
- (4) Motor paralysis of the part.

TABLE I
CLINICAL SUBGROUPS IN PRIMARY LYMPHOEDEMA

Subgroup	Age at onset	Incidence in primary lymphoedema
Lymphoedema congenita ..	Birth	10%
Lymphoedema praecox ..	Before 35 yrs.	80%
Lymphoedema tarda	After 35 yrs.	10%

Primary Lymphoedema

In primary lymphoedema the swelling arises spontaneously and insidiously and there is no evidence of acquired disease. The age at onset of the oedema can be used to subdivide primary lymphoedema into three clinical groups, as shown in Table I. The incidence of the three groups is taken from a series of patients recently analysed by Kinmonth, Taylor *et al.* (1957). Primary lymphoedema is three times more common in women than in men, and a family history of similar disease is present in about 20 per cent. of patients. The term Milroy's disease is often loosely applied to this condition, but to conform with Milroy's original description it should be reserved for primary lymphoedema that is both clinically congenital and familial. It can be seen from Table I that the subgroup lymphoedema praecox has the highest clinical incidence. The typical patient with primary lymphoedema is an adolescent girl or young woman in her twenties with spontaneous oedema of one or both legs. The progression of the swelling is usually slow and initially there may be nothing more than a slight puffiness around the ankle which disappears after a night's rest, only to return as the next day wears on. Hot weather worsens the swelling and an increase is also often noticed just before menstruation. Untreated, the oedema slowly pro-

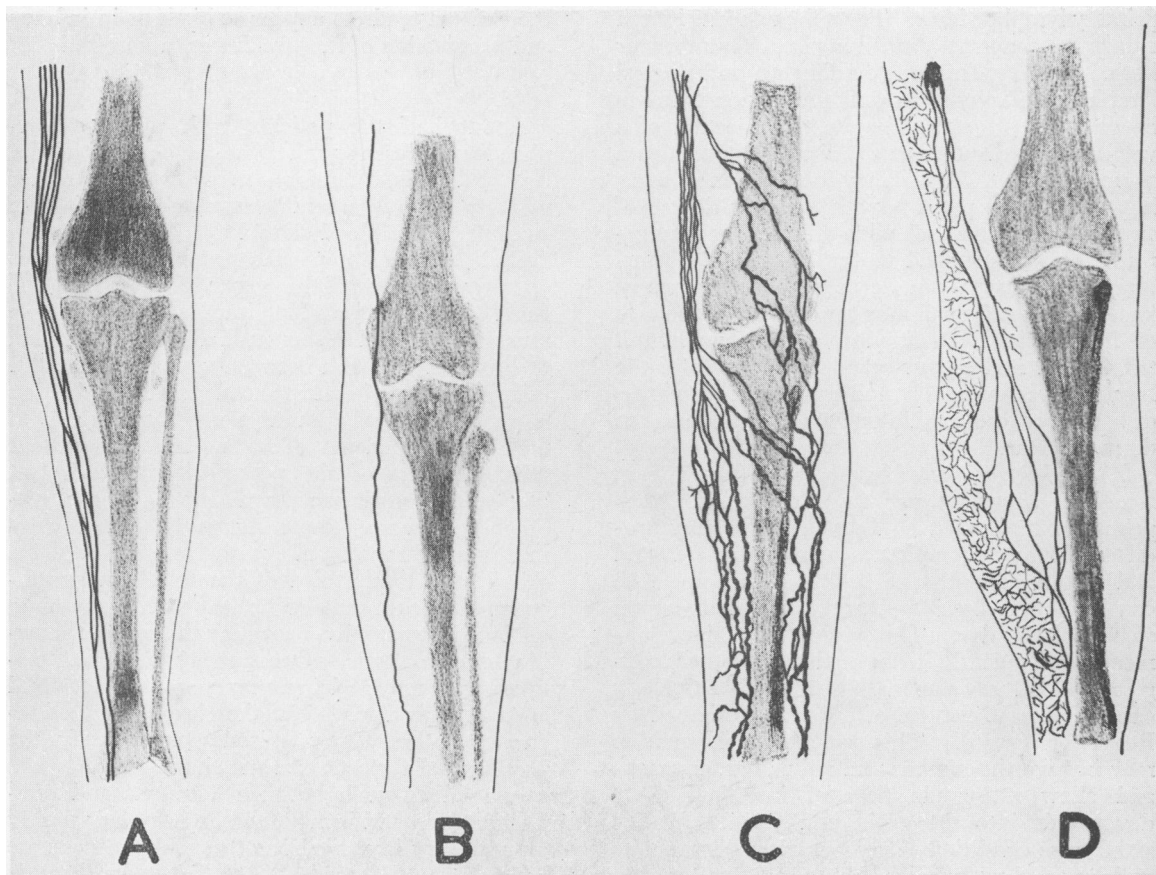


FIG. 1.—Diagram of typical X-ray lymphangiograms. (a) Normal lymphangiogram showing bifurcating arrangement of superficial lymph trunks. (b) Solitary hypoplasia in primary lymphoedema. (c) Varicose lymphatics in primary lymphoedema. (d) Secondary or obstructive lymphoedema. The lymphatics stop at the site of obstruction and there is pooling and dermal back flow of dye.

gresses, until after a varying period of time the whole limb may become grossly swollen. In the early stage symptoms are few. In contrast to post-phlebotic oedema, the lymphoedematous limb is painless and, apart from the development of hyperkeratosis and sometimes damage by recurrent cellulitis, the skin remains relatively normal. The initial complaint is largely cosmetic, but eventually the swollen leg may become heavy and burdensome. Patients with lymphoedema of any origin are prone to recurrent cellulitis in the swollen tissues and this may be a troublesome feature in the more advanced disease. Clinically, there is nothing characteristic about early primary lymphoedema. The oedema is soft, pits easily and is vanquished by a night's rest. In the later stages the high protein content of the oedema fluid produces secondary fibrosis in the subcutaneous tissues, pitting no longer occurs, and there is less

fluctuation with posture. It is in this stage that hyperkeratosis may develop and is often seen on the toes as multiple fine papillary projections.

The Lymphatic Fault

Visual and radiological lymphangiography has shown that in primary lymphoedema the site of the lymphatic defect lies in the main subcutaneous lymph trunks; three main types of abnormality have been found.

(1) *Aplasia* of the lymph trunks occurs in about 17 per cent. of patients with primary lymphoedema. No formed lymph trunks can be found on lymphangiography and this abnormality is often associated with congenital and severe lymphoedema.

(2) *Hypoplasia* of the lymphatic trunks. This is the most common variety of maldevelopment and is found in about 60 per cent. of patients with

primary lymphoedema. The subcutaneous lymph trunks are abnormally small in size, or number, or both. A very frequent finding on radiological lymphangiography is for only one lymph trunk to be outlined (Fig. 1b), despite the injection of a volume of dye sufficient to fill many trunks in a normal subject. This may be termed solitary hypoplasia. In patients with a minor degree of swelling of the foot and ankle this solitary arrangement may be confined to the leg, and a normal lymphatic pattern can be seen to commence at knee level. In a small number of patients the area of hypoplasia is confined to the pelvic lymph trunks and nodes, and lymphangiography of the leg will reveal normal lymph trunks but with areas of back flow of the radio-opaque material into the dermal plexus.

(3) *Varicose or dilated lymph trunks* (Fig. 1c) are found in about 15 per cent. of patients with primary lymphoedema. Lymphangiography produces a spectacular picture of numerous dilated and tortuous lymphatics in which incompetence can be shown by abnormal backward or lateral spread of the dye. This variety of maldevelopment is frequently associated with other congenital blood vascular malformations, particularly congenital A.V. fistulae of the type described by Robertson (1956). This type of malformation may involve the lumbar and pelvic lymph trunks and allow retrograde flow of intestinal chyle downwards into the groin and thigh. In this rather rare condition of chylous reflux, lymphatic vesicles filled with milky chyle appear on the skin of the perineum and thigh. These may rupture, causing a troublesome leak of chylous fluid.

Aetiology

It is believed that the principle aetiological factor in primary lymphoedema is a congenital maldevelopment of the subcutaneous lymph trunks. The evidence for this has been discussed previously (Kinmonth, Taylor *et al.*, 1957). Although the lymphatic defects are of congenital origin the clinical manifestations of oedema may be delayed until adolescence (lymphoedema praecox) or even late adult life (lymphoedema tarda). The reason for this latency is not fully understood but to a certain extent it is related to the severity of the malformation. In lesser degrees of abnormality, such as hypoplasia, lymphatic function is sufficient to cope until perhaps overwhelmed by some factor which in normal subjects would produce oedema of very short duration. Thus the onset of swelling sometimes dates from such trivial events as minor trauma, insect bites, etc. More often, however, there is no clear history of a precipitating incident. Conversely, in the more serious abnormalities, such as aplasia or varicosity of the lymph trunks,

the oedema tends to appear at birth or in infancy and progression of the swelling is more rapid.

Diagnosis

About half the patients with primary lymphoedema present with bilateral oedema of the legs and it is, therefore, necessary to consider whether there is a cardiac or renal cause for the swelling. The blood should also be examined to exclude anaemia or plasma protein deficiency as operative factors. If these systemic lesions can be ruled out, or if the swelling is unilateral the disease must be local, and the common diagnostic problem then is to distinguish between venous disease and lymphoedema. In chronic oedema the distinction is easy on clinical grounds alone, for it is rare to find venous oedema of some duration without other stigmata of the post-phlebitic syndrome. The skin changes are the diagnostic key. Post-phlebitic oedema almost invariably leads to pigmentation, atrophy and eventual ulceration of the skin in the lower third of the legs. In lymphoedema the skin remains healthy and, if anything, tends to hypertrophy, becoming thicker and showing hyperkeratosis. Occasionally recurrent cellulitis in lymphoedema may result in localized areas of skin damage but the clear history of recurrent inflammatory episodes will clarify the problem. In recent oedema, however, it is less easy to distinguish between a venous and lymphatic origin and it may then be necessary to rely on accessory investigations to enable an accurate diagnosis to be made. At this stage there is nothing characteristic about the swelling itself and skin changes will not have developed in venous disease. Three investigations are useful in making the distinction:—

(1) *Lymphangiography*. This investigation, which has been described in detail elsewhere (Kinmonth and Taylor, 1955; Taylor and Kinmonth, 1958), is of considerable value in the diagnosis of limb oedema, and in primary lymphoedema will also provide a prognostic guide according to the type of lymphatic abnormality discovered. In doubtful cases it is the most certain way of demonstrating or excluding lymphatic pathology. A warning may be given here of attempting lymphangiography in the presence of gross oedema of the dorsum of the foot at the site of the exploratory incision. If these tissues are waterlogged at the time of investigation the patent blue will not enter the lymphatics and a fallacious interpretation of lymphatic aplasia may be made. It is worth-while, therefore, to diminish oedema at this site by elevation and compression bandaging before lymphangiography is attempted.

(2) *Analysis of the protein content* of the oedema fluid. Oedema fluid can be collected relatively

easily by the insertion of a fine bore Southey's tube with the limb in a dependent position. An analysis of the protein content of this fluid gives a useful guide to the nature of the oedema. In general, a protein content of 1.5 g. per cent. or over is characteristic of lymphoedema, while the protein level in venous oedema is usually under 1 g. per cent. (Crocket, 1956; Taylor, 1958).

(3) *Investigation of the venous system* by phlebography or infra-red photography. The latter investigation is simple and will often reveal superficial vein dilatation and collateral vein formation which is not apparent to the unaided eye.

Prognosis and Treatment

The prognosis varies with the type of lymphatic malformation. In general, the oedema is greatest and its progression more rapid in those patients with either lymphatic aplasia or varicose lymphatics. Fortunately, the prognosis is more favourable in patients with the most frequently found malformation, that of hypoplasia. The oedema in these patients does not usually manifest itself until early adult life and untreated the increase in the swelling is slow. Conservative management will often halt the progression of the oedema and two simple measures are the main features of this regime. They are:—

(1) Night elevation of the limb by raising the foot end of the bed on blocks at least 12 in. high (pillows under the mattress are inadequate).

(2) The careful fitting and constant wearing of heavy-duty elastic stockings.

The majority of patients, after having the nature of their disease and its natural history explained to them, accept these measures willingly and are conscientious in their application. It is worth noting that the supportive stocking should be of heavy quality, preferably one-way stretch, and made accurately to measurements obtained from the limb at its smallest size. It is often necessary to advise several days bed rest before such measurements are taken. This regime in patients with hypoplasia of the subcutaneous lymph trunks will usually stop progression of the oedema and frequently produces a worth-while shrinkage in the girth of the limb. The effectiveness of conservative treatment is inversely proportional to the duration of the swelling. Patients seen within the first few weeks of onset respond very well and in some of them the local *status quo* can be restored and they will be able to manage eventually without continued support. Conversely, in long-standing lymphoedema secondary fibrosis in the subcutaneous tissue may severely limit the amount of shrinkage, although progression of oedema can usually be prevented. Recurrent cellulitis is often troublesome in lympho-

phoedema and in our experience is always secondary to the lymphatic fault and is not a primary factor in the production of the disease. This complication can be prevented by carefully treating interdigital tinea, which is common in lymphoedema and is often the portal for bacterial entry, and by maintaining susceptible patients on oral penicillin for long periods of time.

Surgical Treatment

Patients with gross swelling of long duration do not often respond to conservative management and the heavy limb constitutes a considerable burden. Function can be greatly improved by an excisional operation of the type first described by Charles (1912). In this procedure, the skin and swollen subcutaneous tissues are excised completely, including the deep fascia if it is thickened and fibrotic. The bared muscle and periosteum are then covered with a thick split-thickness skin graft. This operation removes surgically the tissues draining into the faulty lymph trunks and the post-operative results are good, provided the skin cover remains stable and healthy. The choice of donor site for the skin graft is, therefore, of importance and the skin of the swollen leg should only be used if it is healthy. If there is much hyperkeratosis or if vascular naevi are present the skin should not be used. Recurrent cellulitis may have destroyed the dermal lymph plexus and this skin also does badly as a permanent graft. The adequacy of the dermal lymphatic plexus can be tested by an intradermal injection of patent blue violet and this should be done if there is doubt as to the suitability of the local skin. Destruction of the network is indicated by failure of the dye to spread in a reticular fashion (Butcher and Hoover, 1955) and it is then wise to choose another donor site. Several somewhat differing surgical techniques may be used for the Charles operation, and Watson (1953) and Gibson and Tough (1954) have given clear descriptions of their methods. We find it convenient to cut the graft in long strips with an electric dermatome. The strips are then sewn in position over the bared deeper structures. Most patients require only a below knee operation and the junction of the grafted area with the normal tissues should be tapered to avoid an ugly 'plus four' effect. If gross thigh swelling is also present the operation is extended in stages to include this area. It must be realized that the Charles procedure is a major undertaking and, although the functional results are good, the resulting over-thin leg is not always cosmetically pleasing. For these reasons it should not be done for cosmetic reasons in lesser degrees of oedema and the best results are obtained in limbs swollen sufficiently to impose a functional burden on the patient.

In *chylous reflux* the profuse leakage of chyle from ruptured cutaneous vesicles is often a serious handicap to the patient, although the loss of chyle is rarely sufficient to cause constitutional upset. Retro-peritoneal ligation of the dilated and incompetent pelvic lymphatics is the treatment of choice. An injection of patent blue given into the legs prior to operation will colour the pelvic lymph trunks and make subsequent identification easier. The lymphatic malformation is often very extensive and more than one exploration may be required.

Secondary or Obstructive Lymphoedema

Involvement of the lymphatic channels and nodes by inflammatory or neoplastic disease or their surgical excision, as in block dissection of the axilla or groin, may be followed by lymphoedema of the distal tissues. The progression of the oedema is generally more rapid than in primary lymphoedema and the limb soon becomes burdensome. As in primary lymphoedema, secondary cellulitis may occur with distressing frequency. The diagnosis is generally made easily with the knowledge of the primary condition, but sometimes there is doubt as to whether venous or lymphatic involvement is responsible for the swelling. Lymphangiography in secondary lymphoedema gives a characteristic appearance whatever the obstructing agent. On interdigital injection of patent blue, pronounced dermal back flow of the dye will be seen in the limb proximal to the injection site and radiological lymphangiography confirms this finding. The X-ray appearance is of relatively normal main trunks, with little or no dilatation, which come to a stop at the site of the obstruction. In addition, the back flow of radio-opaque material into the dermal lymphatic plexus shows as a characteristic diffuse reticular pattern (Fig. 1d).

Post-mastectomy oedema is a not infrequent example of secondary lymphoedema, and lymphangiography in this condition gives the typical picture of secondary lymphoedema. Dermal back flow is seen in the arm and the lymph trunks can be seen to stop at axillary level.

Treatment

Treatment in secondary lymphoedema depends largely on the nature of the obstructing agent, but in those patients in whom the original disease is inactive the oedema may require treatment on its own merits. In theory, lymphangioplasty is an attractive proposition in secondary lymphoedema and numerous unsuccessful attempts have been made to insert artificial conducting channels across the region of obstruction to areas with normal lymphatic drainage. Gillies and Fraser (1935)



FIG. 2.—Lymphangiosarcoma developing in primary lymphoedema of the leg. (Mr. D. F. Ellison Nash's case.)

described an operation in which a pedicle graft was used to bridge an area of lymphatic obstruction and, while this operation will not succeed in primary lymphoedema where the lymphatic malformation is widespread, it may be of benefit in the secondary lymphoedema that follows a localized destruction of main lymphatic channels. The Charles operation, however, again offers the best prospect of permanent relief from troublesome secondary lymphoedema, providing the original disease is inactive and the general prognosis good.

Lymphangiosarcoma in Lymphoedema

This fatal complication of chronic lymphoedema (Fig. 2) has been reported frequently in recent years (Stewart and Treves, 1948; Kettle, 1957). It occurs most often in post-mastectomy oedema but has also been observed in primary lymphoedema of the legs (Martorell, 1951). The neoplastic change usually occurs in lymphoedema of some years standing. Reddish-purple nodules of firm consistency appear in the oedematous skin and spread rapidly to form a confluent mass. Satellite nodules soon develop and remote metas-

tases occur from blood-vessel involvement. The clinical appearance of the lesions resembles that of Kaposi's angiosarcoma but the histological picture enables the distinction to be made. The majority of the reported patients have been treated by radical amputation, but without success. The tumour is moderately radiosensitive and radiotherapy is probably the treatment of choice.

REFERENCES

- BUTCHER, H. R., and Hoover, A. L. (1955), *Ann. Surg.*, **142**, 633.
 CHARLES, H. (1912), 'A System of Treatment, ed. Latham and English. London. J. & A. Churchill.
 CROCKET, D. J. (1956), *Lancet*, **ii**, 1179.
 GIBSON, T., and TOUGH, J. S. (1954), *Brit. J. plast. Surg.*, **7**, 195.
 GILLIES, H., and FRASER, F. R. (1935), *Brit. med. J.*, **i**, 96.
 KETTLE, H. J. (1957), *Brit. med. J.*, **i**, 193.
 KINMONTH, J. B., TAYLOR, G. W., and HARPER, R. A. K. (1955), *Brit. med. J.*, **i**, 940.
 KINMONTH, J. B., TAYLOR, G. W., TRACY, G. D., and MARSH, J. D. (1957), *Brit. J. Surg.*, **45**, 1.
 MARTORELL, F. (1951), *Angiology*, **2**, 386.
 ROBERTSON, D. J. (1956), *Ann. roy. Coll. Surg. Eng.*, **18**, 73.
 STEWART, F. E., and TREVES, N. (1948), *Cancer*, **1**, 64.
 TAYLOR, G. W., and KINMONTH, J. B. (1958), 'Recent Advances in Surgery, edit. Selwyn Taylor. Churchill. London (in press).
 WATSON, J. (1953), *Brit. J. Surg.*, **41**, 31.

THYROID DISEASE

Price: 4s. 0d., post free

DIAGNOSTIC PROCEDURES IN THYROID DISEASE

Russell Fraser, M.D., F.R.C.P., D.P.M.

THE PLACE OF RADIOACTIVE IODINE IN THE TREATMENT OF THYROID DISEASE

E. E. Pochin, M.D., F.R.C.P.

ANTITHYROID DRUGS

James Crooks, M.B., M.R.C.P. (Lond. and Ed.), F.R.F.P.S.G.

SUBACUTE THYROIDITIS

Selwyn Taylor, M.Ch., F.R.C.S.

RECENT WORK ON THYROID HORMONES

J. H. Wilkinson, B.Sc., Ph.D., F.R.I.C.

SOME UNUSUAL MANIFESTATIONS OF THYROID DISEASE

W. R. Trotter, D.M., M.R.C.P.

CARCINOMA OF THE THYROID

John E. Piercy, F.R.C.S., F.R.C.S.E.

LYMPHOID GOITRES

T. Levitt, M.A., F.R.C.S.Eng., F.R.C.S.Ed., F.R.C.S.I.

Published by

THE FELLOWSHIP OF POSTGRADUATE MEDICINE

60, Portland Place, London, W.1